UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,128	02/27/2006	Murray Goodman	041673-3108	1953

30542 7590 03/18/2010

FOLEY & LARDNER LLP
P.O. BOX 80278
SAN DIEGO, CA 92138-0278

EXAMINER	
SILVERMAN, ERIC E	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
03/18/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,128	GOODMAN ET AL.	
	Examiner	Art Unit	
	ERIC E. SILVERMAN	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above claim(s) *5,6,11-23,26-28 and 31-57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-10,24,25,29 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :12/30/09 9/18/07 8/11/05 5/23/05.

DETAILED ACTION

Election/Restrictions

Claims 31-57 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/9/09. The traversal is on the ground(s) that the claims were restricted into too many groups and that there is no search burden to search at least some of the groups together. This is not found persuasive because the number of groups into which the election is restricted has no bearing on whether or not restriction is proper. Further, this Application was filed under section 371, so the unity of invention standard applies to restriction requirements. Search burden is not a criterion in the unity of invention standard.

Applicant also traversed requirement for election of a species of single dendrimer and single active agent. The traversal was on the basis that the dendrimer of claim 1 is novel, and so search of additional actives is not burdensome. In response, the dendrimer of claim 1 is not novel (see below), and search burden is not germane to the lack of unity standard.

The requirement is still deemed proper and is therefore made **FINAL**.

Applicant elected the dendrimer of claim 17 and the drug methotrexate. Applicant submitted that the claims reading on the elected species are claims 1-15, 17, 24, 25, 29, and 30. The Examiner notes, however, the claims 5 and 6 does not read on the elected dendrimer of claim 17. Claims 5 and 6 require, respectively, at least 3 or 4

tetravelent atoms, each tetravalent atom bound to at least three groups bearing the specified terminal groups, which may be guanidine for example. That means that claims 5 and 6 require dendrimers having, respectively, at least 9 or 12 guanidine groups (or other listed terminal groups). The dendrimer of claim 17 has only six guanidine groups - the open valence is for binding of the drug (the elected drug is methotrexate). Furthermore, the only such tetravalent atoms in the elected dendrimer are the tris(hydroxymethyl)aminomethane atoms, and there are only two of such atoms in the elected dendrimer.

Allowable Subject Matter

The elected species (the dendrimer of claim 17 wherein the open valence is a covelent bond to methotrexate with no linker between the methotrexate and the amide) is allowable. The search was expanded to cover the dendrimer of claim 17 wherein the open valence is a direct covalent bond to other drugs (again with no linker). This is also allowable. The search was then expanded to arginine based dendrimers covalently bound to the elected drug methotrexate. This was found in the art, and so the search was not further expanded. Claims not included in the species that was found are withdrawn from consideration. MPEP 802.03. Claims 1-4, 7-10, 24, 25, 29, and 30 are treated on the merits; claims 5, 6, 11-28, and 31-57 are withdrawn.

In the interest of compact prosecution, all of the prior art that was found during the expanded search applied against the claims in this action. Art that is applicable only against the generic claims but not against the last species searched is applied against those claims to which it is applicable.

Claim Objections

Claims 24, 25, 29 and 30 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim may not depend from another multiple dependent claim. See MPEP § 608.01(n). While claim 30 is not a multiple dependent claim, it depends from improper claim 29 and therefore is also subject to this objection. Accordingly, these claims have not been further treated on the merits.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-4 and 7-10 are rejected under 35 U.S.C. 102(a) as being anticipated by Kasai et al. (cited on 892)

The Office has determined that the Kasai reference was publicly available no later than March 25, 2002; that is the publication date of the issue of Biooranic and Medicinal Chemistry Letters containing the article.

The lysine and arginine based dendrimers TX-1944 and TX-1943 read on the instant claims. TX-1943 and TX-1944 have anti-angiogenic activity. Page 953, right col. Thus, at least part of those dendrimers is a bioactive molecule. Further, the guanidino groups bind to heparin, which is a known bioactive molecule. Page 953-54.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 and 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kasai in view of Liu et al. (cited on 892) and Ryser et al. (cited on IDS).

Kasai was discussed above.

Kasai does not teach methotrexate bound to the core of the dendrimer.

Liu teaches that the internal cavity of a dendrimer can be used for entrapment of drugs with the possibility of controlled release. Page 396. The strategies of encapsulation suggested in Liu involve entrapping the drug near the core; Liu discusses: physical entrapment through the dendrons; non-covalent hydrophilic interactions, such as hydrogen bonding, with the core; and hydrophobic interactions between the drug and the core. Pages 396-97.

Ryser teaches that methotrexate may be covalently bound to polylysine to increase the transport of the drug and overcome drug resistance.

It would have been prima facie obvious to a person of ordinary skill in the art at the time of the invention to covalently bind methotrexate to the core of the lysine based Kasai dendrimer. The artisan would do this because of an expectation that the resultant molecule would have increased drug transport, and would overcome drug resistance. Further, because methotrexate is an anti-cancer agent, combining it with an antiangiogenesis carrier (the Kasai dendrimer) would be helpful in treating cancer or in addressing the side effects of chemotherapy. Also, the artisan would anticipate the possibility of controlled release from the resulting molecule.

The artisan would expect success in making this molecule. The dendrimer of Kasai has a carboxylic acid group in the core that can serve as a synthetic handle for attachment of methotrexate. Further, Ryser teaches how to attach methotrexate to polylysine by using carbodiimide to activate a carboxylyic acid; a similar strategy would likely succeed with the Kasai dendrimer.

Conclusion

The allowable subject matter in this application is discussed above. No claims are currently allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERIC E. SILVERMAN whose telephone number is (571)272-5549. The examiner can normally be reached on Monday to Thursday 7:00 am to 5:00 pm and Friday 7:00 am to noon.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571 272 0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric E Silverman/
Primary Examiner, Art Unit 1618